REMARKS

Claims 1-21 and 23-24 are pending in the instant application. Claims 7 and 11-24 are withdrawn from consideration while the remaining claims 1-6 and 8-10 are rejected. The Examiner makes the Restriction Requirement final. The recitations of claims 4 and 5 are combined into claim 1. Claims 8 and 9 are changed to depend from claim 1. Thus, upon entry of the instant Amendment and Response, claims 1-3, 6-21 and 23-24 will be pending.

As a preliminary matter, Applicants retransmit the "Request for Withdrawal of Attorney of Record" submitted on December 19, 2007 by Steven J. Hultquist, Esq., The Request was not approved in a Decision on Petition to Withdraw, mailed from the USPTO on February 4, 2008. Applicants are not seeking any review of this decision. Applicants merely wish to clarify that all further communication should be sent to the undersigned. Applicants submitted a Revocation of Power of Attorney and Authorization of Agent on October 18, 2007 requesting that all future correspondence be sent to the undersigned. However, the Office Action mailed on December 12, 2007 was inadvertently mailed to the previous attorney of record whose power of attorney had already been revoked.

Objection to the Specification

The Examiner objects to the specification because of the following:

(i) The Brief Description of the Drawings does not reference each of the Figures, and it should be amended to reference Figures 17 A, 17B, 18A, 18B, 21 A, 21 B, 22A, 22B, 23A, and 23B;

(ii) The Brief Description for Figure 19c mentions (a) and (b), which are not found in Figure 19c;

(iii) The Brief Description for Figure 27 describes (a), (b), (c) and (d), however, only (a), (b) and (c) are found in Figure 27; and

(iv) The Brief Description for Figure 29 (e,f) describes (d) and (e) instead of (e) and

(f).

Applicants herein provide amended text to correct these matters. No issue of new matter arises since the corrections are purely formalities and represent obvious corrections of grammatical errors. Applicants use the paragraph numbering present in the published United States application.

Objection to the Claims

Claims 2, 3, and 8 are objected to because of the following informalities:

(i) Claim 2 is objected to for reciting the term "other cells." It is unclear what cells the term refers to;

(ii) Claim 3 is allegedly unclear in reciting "isolating the gel band of the protein" as it is allegedly unclear which gel band is intended;

(iii) Claim 8 is objected to because it depends from a non-elected claim (claim 7).

Applicants herein remove the offending recitation "and other cells" from claim 2 as it is unnecessary to describe the invention, and removing the term does not affect the scope of the claims. Applicants change the article "the" to the indefinite article "a" to introduce the recitation "gel band" thereby obviating the objection. Applicants amend claim 8 so that it no longer depends from non-elected claim 7 but rather actively recites the steps of the methods of claim 7, i.e. effectively incorporates the recitations of claim 7. Thus, this objection is moot.

Rejection under 35 USC §101

The Examiner rejects claims 1-5 under 35 U.S.C. § 101 as allegedly directed to non-statutory subject matter. Claims 1-5, as written, allegedly do not sufficiently distinguish over glycoproteins as they exist naturally. The Examiner correctly notes that when purification results in a new utility, patentability is considered. Applicants herein amend claims 1 and 2 (and by virtue of dependency therefrom, the remaining dependent claims) to recite "an isolated"

glycoprotein as the Examiner suggests to obviate this rejection.

Rejection under 35 USC §112, second paragraph

The Examiner rejects claim 2 under 35 U.S.C. 112, second paragraph, as allegedly unclear because of the phrase "functional derivative or active fraction thereof" as the meaning of "derivative" is unclear. Allegedly, it is unclear what function and activity the "derivatives" have. Applicants respectfully traverse. Applicants respectfully refer the Examiner to page 15, first full paragraph of the present specification wherein Applicants provide a clear definition of "functional derivatives" and teach how one of ordinary skill in the art may select such derivatives having substantially the same biological activity as ACA. Applicants clearly define these "functional derivatives" as "derivatives having substantially the same biological activity as ACA." As such, Applicants submit that claim 2 is clear and definitely describes the invention.

Rejection under 35 USC §112, first paragraph

1. Regarding Written Description

The Examiner rejects claims 2-6 and 8-10 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Allegedly, the claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. This rejection is made because:

i) Applicants are claiming a genus of molecules having part or all characteristics recited in the claims, as well as functional derivatives and active fractions thereof while the specification only describes one ACA glycoprotein; and

ii) Applicants are claiming a recombinant protein while the specification only discloses a partial amino acid sequence for the protein.

Claims 2-6, and 9-10 depend from claim 1 and are directed to surface glycoproteins having

additional features. Claim 8 is drawn to a surface glycoprotein ACA that is obtained from human blood and characterized by the molecular weight of 65 or 68 kDa. The Examiner admits that the GPI-anchored proteins having the characteristics of claim 1 are well known in the art. However, the Examiner says that glycoproteins having the additional characteristics of clams 2-6, and 8-10 are not known. Moreover, as only one species is described, the only glycoproteins described have all the features of the claims and not only part of the features. In addition, regarding "functional derivatives and active fragments," no biological derivative or active fragment has been described. Therefore, according to the Examiner, only the ACA protein has all the features recited in claims 2-5 (GPI anchored, obtained from human blood, isoelectric point, molecular weight, comprising SEQ ID NO.1-11), but not the full breadth of a surface glycoprotein ACA, functional derivatives, and active fragments thereof meet the written description requirement. Still further, the Examiner says that Applicants are not in possession of the claimed recombinant protein since claims 8 and 9 are drawn to a recombinant protein of a surface glycoprotein ACA, for only a partial sequence is provided.

In the interest of advancing prosecution and more clearly defining the invention, Applicants herein combine claims 4 and 5 with claim 1. As a result of this change, Applicants more clearly define characteristics of the isolated surface glycoproteins which they clearly possess and describe with such particularity so as to demonstrate possession thereof.

As regards the Examiner's allegations that Applicants are not in possession of the recombinant proteins embraced by claims 8 and 9 since only partial amino acid sequences are provided but no DNA sequences are provided, Applicants respectfully remind the Examiner that as of the filing date of the present application, one of ordinary skill in the art could easily design probes to screen the genomic or cDNA libraries based upon the various partial amino acid sequences disclosed. Hence, Applicants submit that one of ordinary skill in the art could derive the DNA encoding the protein and produce the recombinant protein. In addition, Applicants submit that the specification teaches at least two monoclonal antibodies against ACA. Therefore, one of ordinary skill in the art could screen an

expression library such as a human phage display cDNA library and select clones expressing ACA. Still further, Applicants submit that one of ordinary skill in the art could use bioinformatics to find the DNA sequence of the gene encoding ACA in already existing gene banks or protein banks.

2. Regarding Enablement

The Examiner rejects claims 2-6 and 8-10 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the surface glycoprotein ACA, a salt thereof that is characterized by ***all*** the features recited in claims 2-6 and 8-10, does not reasonably enable any and all surface glycoprotein ACA, functional derivatives, active fragments, and recombinant proteins thereof that is characterized by the features disclosed in claims 2-5 and 8-10. According to the Examiner, Applicants are claiming a genus of molecules including any and all ACA glycoproteins having part or all of the features recited in the claims, functional derivatives, active fragments, and recombinant proteins thereof.

Applicants refer to the well settled legal test that governs whether an application meets the requirements of 35 U.S.C. 112, first paragraph regarding enablement as articulated by the court of, for instance, *In re Wands*. The relevant question is "whether one of ordinary skill in the art can practice (make and use) the invention without undue experimentation." The court of *In re Wands* settled that a great deal of experimentation may be required before the threshold to "undue experimentation" is crossed.

As set forth above, in the interest of advancing prosecution and more clearly defining the invention, Applicants herein combine claims 4 and 5 with claim 1. As a result of this change, Applicants more clearly define characteristics of the isolated surface glycoproteins. Applicants submit that one of ordinary skill in the art could make and use these isolated surface glycoproteins without undue experimentation.

As regards the recombinant proteins embraced by claims 8 and 9 for which only partial amino acid sequences are provided but no DNA sequences are provided, Applicants respectfully remind the Examiner that as of the filing date of the present application, one of ordinary skill in the art could easily design probes to screen the genomic or cDNA libraries based upon the various partial amino acid sequences disclosed. Hence, Applicants submit

that one of ordinary skill in the art could derive the DNA encoding the protein and produce the recombinant protein. In addition, Applicants submit that the specification teaches at least two monoclonal antibodies against ACA. Therefore, one of ordinary skill in the art could screen an expression library such as a human phage display cDNA library and select clones expressing ACA. Still further, Applicants submit that one of ordinary skill in the art could use bioinformatics to find the DNA sequence of the gene encoding ACA in already existing gene banks or protein banks. None of the foregoing efforts require undue experimentation by one of ordinary skill in the art but rather represent no more than routine screening.

Rejection under* 35 *USC* § *102

1. U.S. Patent No. 5,519,120 as evidenced by Chen *et al.*, *PNAS* 1998, 95: 9512-9517

The Examiner rejects claims 1 and 8 under 35 U.S.C. 102(b) as allegedly anticipated by U.S. Patent No. 5,519,120 as evidenced by Chen *et al.*, *PNAS* 1998, 95: 9512-9517. US 5,519,120 allegedly teaches a GPI-anchored protein fl-PAR which can be removed from the cell surface by treatment with PI-PLC (citing Columns 55-56). It allegedly further teaches that the majority of the GPI-anchored proteins are susceptible to PI-PLC, which releases the proteins into the medium by removing the diacylglycerol portion of the glycolipid (citing Column 55, lines 54-60). According to the Examiner, because μ-PAR can be removed by the treatment of PI-PLC, its GPI-anchor would have a non-acetylated inositol ring as evidenced by Chen *et al.* Chen *et al.* allegedly teach that the PI-PLC resistance of a GPI-anchored protein is due to acetylation of an inositol hydroxyl group (*citing* page 9512, left column, last paragraph). Moreover, the Examiner says that U.S. Patent No. 5,519,120 teaches treating cells with PI-PLC (*citing* column 55-56), the proteins, which are released into the medium by PI-PLC treatment, include all the GPI-anchored proteins that are present on the cell surface. Such GPI-anchored proteins would include those that are characterized by a non-acetylated inositol ring and diacyl glycerol as lipid tail of the anchor. Therefore, U.S. Patent No. 5,519,120 allegedly teaches all the limitations of claim 1.

U.S. Patent No. 5,519,120 allegedly further teaches that the μ-PAR was originally

identified in blood monocytes (*citing* column 3, lines 421-43). US 5,519,120 teaches that the molecular weight of μ-PAR detected by SOS-PAGE under reducing condition using an antibody is about 67 kD (covering 65-68 Kd region, see Figures 4A and 5A, and column 47, line 43). Claim 8 is a product by process claim.

According to the Examiner, the product WPAR of the prior art appears to be the same as the product of claim 8 because they both are isolated from blood cells and have the same molecular weight. Moreover, the claims do not define that manufacturing process steps impart any distinctive structural characteristics to the final product compared to the product in the prior art, the patentability of the product cited in claim 8 does not depend on its method of production.

As set forth above, Applicants herein combine the recitations of claims 4 and 5 into claim 1. Moreover, Applicants further amend claim 8 to depend from claim 1 so that all the recitations of claim 1 are incorporated into claim 8. U.S. Patent No. 5,519,120 teaches a glycoprotein having a molecular weight of only 55-60 kDa as determined by SDS-PAGE. (*See*, Figures 5A and 5B) U.S. Patent No. 5,519,120 does not teach or suggest a glycoprotein having a molecular weight of about 65 kDa or 68 kDa as currently claimed. Moreover, U.S. Patent No. 5,519,120 does not teach or suggest any of the sequences recited in claim 1 as incorporated from claim 5 (now canceled). For this additional reason, the presently claimed invention is patentable.

2. Harada *et al.*, *Glycoconj. J.* 1992, Aug., 9(4): 198-203

The Examiner rejects claim 8 under 35 U.S.C. 102(b) as allegedly anticipated by Harada *et al., Glycoconj. J.* 1992, Aug., 9(4): 198-203. The Examiner says that Harada *et al.* teach a surface glycoprotein that is isolated from human blood cells, i.e. natural killer cells and has a molecular weight of 65 kDa as determined by SDS-PAGE gel under reducing condition (citing Abstract, and page 199, 1st column, 3rd paragraph). According to the Examiner, the surface glycoprotein disclosed by Harada *et al.* appears to be the same as the product of claim 8 because they both are isolated from blood cells and have the same molecular weight. Moreover, the claims do not define that manufacturing process steps impart any distinctive structural characteristics to the final product compared to the product in the prior art, the patentability of the product cited in claim 8 does not depend on its method of production.

As set forth above, Applicants herein combine the recitations of claims 4 and 5 into claim 1 and change claim 8 to depend from the amended claim 1. Therefore, claim 8 includes all the recitations of previously presented claims 1, 4 and 5. Harada *et al.,* do not teach or suggest a glycoprotein having a molecular weight of about 65 kDa or 68 kDa as currently claimed. Moreover, Harada *et al.,* do not teach or suggest any of the sequences recited in claim 1 as incorporated from claim 5 (now canceled). Hence, the presently claimed invention is patentable. Moreover, Harada *et al.* teach a protein having a pI in the range of 4.1 to 4.6. (*See*, Abstract, page 198) The proteins of the present invention as described in claim 2 have an isoelectric point of 5.5. For this additional reason, the presently claimed invention is patentable.

3. Kroumpouzos *et al., J. Invest. Oermatol.,* 1996, 106(4): 623 as evidenced by Chen *et al., PNAS* 1998, 95: 9512-9517

The Examiner rejects claim 1 under 35 U.S.C. 102(b) as allegedly anticipated by Kroumpouzos *et al., J. Invest. Oermatol.*, 1996, 106(4):623 as evidenced by Chen *et al. PNAS* 1998, 95: 9512-9517. The Examiner says that Kroumpouzos *et al.* teach a 65 kO membrane GPI-glycoprotein which is isolated from malignant melanoma, is overexpressed in melanoma tissues as compared to normal tissues, has diacylglycerol as a lipid structure of GPI anchor and is sensitive to phospholipase PI-PLC. According to the Examiner, because the protein of Kroumpouzos *et al.* is sensitive to PI- PLC, its GPI-anchor would have a non-acetylated inositol ring as evidenced by Chen *et al.* Further, allegedly Chen *et al.* teach that the PI-PLC resistance of a GPI-anchored protein is due to acetylation of an inositol hydroxyl group (citing page 9512, left column, last paragraph).

As set forth above, Applicants herein combine the recitations of claims 4 and 5 into claim 1. Kroumpouzos *et al.* do not teach or suggest a glycoprotein having a molecular weight of about 65 kDa or 68 kDa as currently claimed. Moreover, Kroumpouzos *et al.* do not teach or suggest any of the sequences recited in claim 1 as incorporated from claim 5 (now canceled). For this additional reason, the presently claimed invention is patentable. Even if, *assuming arguendo*, such were not the case, Kroumpouzos *et al.* do not teach one of ordinary skill in the art how to make and use the purified protein disclosed therein. As such, Kroumpouzos *et al.* do not enable their alleged teachings. Therefore, Kroumpouzos *et al.* is not a valid references under

35 U.S.C. 102.

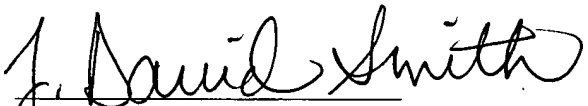
FEES

No additional fees are believed necessary in connection with the present submission, however, should this be in error, authorization is hereby given to charge Deposit Account No. 11-1153 for any underpayment or to credit any overage.

CONCLUSION

It is believed that all of the claims are patentable and early notification as such is earnestly solicited. If any issues may be resolved by way of telephone, the Examiner is invited to call the undersigned at the telephone number indicated below.

Respectfully submitted,



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